UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/086,206	02/28/2002	Juana Magdalena	408.014-CON	1829

20311 7590 12/12/2007

LUCAS & MERCANTI, LLP
475 PARK AVENUE SOUTH
15TH FLOOR
NEW YORK, NY 10016

EXAMINER	
JOHANNSEN, DIANA B	
ART UNIT	**PAPER NUMBER**
1634	

MAIL DATE	DELIVERY MODE
12/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/086,206	MAGDALENA ET AL.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-32,34-38,40,41,44,47,49-52,54 and 55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *36,44 and 54* is/are allowed.

6)☒ Claim(s) *28-31,34,35,37,38,40,41,47,49-52 and 55* is/are rejected.

7)☒ Claim(s) *32* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 30, 2007 has been entered.

2. Claims 28-30, 35-38, 40-41, 44, 47, 49, 52, and 54-55 have been amended and claims 39, 42-43, 48 and 53 have been canceled. Claims 28-32, 34-38, 40-41, 44, 47, 49-52 and 54-55 are now pending and under consideration. Any prior rejection and/or objection not reiterated herein has been with withdrawn.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 28-31, 34, 35, 37, 38, 40, 41, 47, 49-51, and 55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids/probes consisting of SEQ ID NOS 1 and 2 and the complements thereof, as well as probes or primers consisting of 24 consecutive nucleotides of SEQ ID NO: 1 or 2 or the complements thereof, a probe consisting of 21 consecutive nucleotides of SEQ ID NO: 2 that includes the GAG codon at positions 40 to 42 (or the complement of such a

probe), a probe consisting of nucleotides 31-51 of SEQ ID NO: 2 (or the complement thereof), and for probes/primers including the previously referenced sequences that have the functional property of specifically hybridizing to and specifically detecting mycobacteria belonging to the *M. tuberculosis* complex, does not reasonably provide enablement for any probes/primers comprising SEQ ID NOS 1 or 2 or 24 mers thereof or the complements thereof and lacking the functional property noted above, or for any "corresponding" RNA sequences or genes (see text of claims 35, 41, and 47), or for a probe that "consists of 21 base pairs having a sequence of a region of sequence SEQ ID NO: 2 comprising the GAG codon in positions 40 to 42 or the complement of said region" (see text of claim 37), or for a probe "comprising a sequence composed of nucleotides in positions 31 to 51 of SEQ ID No: 2 or the complement of said sequence" (see claim 38, as well as claim 55). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make

or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (*MPEP* 2164.01(a)).

Claims 28-31, 35, and 40-41 encompass nucleic acids comprising SEQ ID NOS 1 or 2 or the complements thereof. Claim 34 is drawn to a probe or primer that comprises 24 consecutive nucleotides of SEQ ID NO 1 or 2 or of the complements thereof. Claims 35 and 41 also encompass probes comprising any RNA or gene "corresponding" to SEQ ID NO: 1 or its complement, and claim 41 further comprises probes comprising any RNA or gene "corresponding to SEQ ID NO: 2;" claim 47 and the claims dependent therefrom are drawn to methods employing such probes. Claim 37 is drawn to a probe that "consists of 21 base pairs having a sequence of a region of sequence SEQ ID NO: 2 comprising the GAG codon in positions 40 to 42 or the complement of said region." It is noted that this language broadly encompasses any 21 mer including any sequence obtained from "a region of sequence SEQ ID NO: 2 comprising the GAG codon." Claim 38 is drawn to a probe "comprising a sequence composed of nucleotides in positions 31 to 51 of SEQ ID No: 2 or the complement of said sequence," and claim 55 is drawn to a method employing such a probe. It is noted that this language broadly encompasses any probe that may be "composed of" the recited nucleotides (i.e., the claims do not require, e.g., consecutive nucleotides of SEQ ID NO: 2).

It is unpredictable as to whether one of skill in the art could make and use applicant's invention in a manner reasonably commensurate with the instant claims. The specification discloses particular sequences present in the senX3-regX3 intergenic

region of *M. tuberculosis* complex strains of mycobacteria (SEQ ID NOs 1 and 2) and combinations thereof (e.g., 2 copies of SEQ ID NO: 1 followed by 1 copy of SEQ ID NO: 2) and portions thereof (e.g., nucleotides 31-51 of SEQ ID NO: 2) that are useful in detecting and differentiating mycobacteria of the *M. tuberculosis* complex (see, e.g., Example 5). It is further noted that applicant's have disclosed the full length sequence of the senX3-regX3 intergenic region as well as of the flanking senX3 and regX3 genes (see Figure 2, SEQ ID NO: 12). However, the instant claims broadly encompass any nucleic acids including SEQ ID NO: 1 or 2 or the complements or portions thereof noted above, without any requirement that said nucleic acids be capable of functioning in the detection methods taught by applicant. Rather, the claims encompass, e.g., many thousands of different nucleic acids including any type or amount of flanking sequence, the majority of which sequences could not function in detecting/differentiating *M. tuberculosis* complex mycobacteria. Further, some of applicant's claims (as indicated above) include any gene or RNA that could be considered to "correspond" to this large group of nucleic acids, as well as molecules constructed using only small portions of the particular sequences taught by applicant, or constructed by arranging nucleotides obtained from those sequences in any order. While a skilled artisan could clearly employ in the methods of the invention the specific sequences taught by applicant, as well a small subset of nucleic acids embraced by the claims that include these specific sequences and have the functional property of specifically hybridizing to and specifically detecting mycobacteria belonging to the *M. tuberculosis* complex (as discussed in the specification at, e.g., pages 5 and 12), no quantity of experimentation would enable the

use of the vast majority of the sequences encompassed by the claims in *M. tuberculosis* complex detection. Such a quantity of experimentation is clearly undue. Lacking guidance from the specification, one of skill in the art may look to the teachings of the prior art for further guidance with regard to enablement of a claimed invention. However, in the instant case, the prior art is silent with regard to any probes or primers comprising SEQ ID NO: 1, SEQ ID NO: 2, or the complements, combinations or portions, etc., claimed by applicant and encompassed by the instant claims. Therefore, the teachings of the prior art cannot be relied upon with respect to enablement of the claimed invention either for the uses disclosed by applicant (i.e., detection/differentiation of *M. tuberculosis* complex strains) or for any other use. Thus, while the teachings of the specification enable the preparation and use of nucleic acids/probes consisting of SEQ ID NOS 1 and 2 and the complements thereof, as well as probes or primers consisting of 24 consecutive nucleotides of SEQ ID NO: 1 or 2 or the complements thereof, a probe consisting of 21 consecutive nucleotides of SEQ ID NO: 2 that includes the GAG codon at positions 40 to 42 (or the complement of such a probe), a probe consisting of nucleotides 31-51 of SEQ ID NO: 2 (or the complement thereof), and for probes/primers including the previously referenced sequences that have the functional property of specifically hybridizing to and specifically detecting mycobacteria belonging to the *M. tuberculosis* complex, it would require undue experimentation to make and use applicant's invention in a manner reasonably commensurate with the instant claims.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 47, 49-52, and 55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 47 and 49-51 are indefinite over the references to "step (2)" in item (3) of claim 47 because the claim does not previously employ the term "step" or "step (2)" and does not otherwise make reference to method steps. This rejection could be overcome by, e.g., amending claim 47 to recite "comprising the steps of" (in lieu of "comprising" in line 2).

Claims 50-51 are indefinite because the language of the claims does not make clear how the method may actually be used to "differentiate an infection by BCG from an infection by a virulent mycobacterium of M. tuberculosis complex." It is noted that the method of claim 49 (from which claim 50 depends) achieves the objective of "detecting a mycobacteria strain of *M. tuberculosis* complex." The text of claim 50 does not indicate how such detected allows or is used to achieve the differentiation required by claims 50-51. Clarification is required.

Claims 52 is indefinite over the reference to "step (1)" in item (2) of the claim because the claim does not previously employ the term "step" or "step (1)" and does not otherwise make reference to method steps. This rejection could be overcome by, e.g., amending claim 52 to recite "comprising the steps of" (in lieu of "comprising" in line 2).

Claim 52 is indefinite because it is not clear how the final step of "measuring a length of" amplification products in (2) relates to or results in "identifying groups of

mycobacteria belonging to a M. tuberculosis complex," as set forth in the preamble of the claim. There is no indication in the claim as to how groups of mycobacteria are actually identified. Clarification is required.

Claim 52 is also indefinite over the recitation of the limitation "56 base pairs upstream and 62 base pairs downstream of a sequence selected from...." because it is not clear what sequence containing SEQ ID NO: 1, 2, etc., is referenced by this language, and how or whether this limitation relates to the "DNA of previously extracted strains" of item (1) of the claim. The claim should amended to make clear what molecule or sequence contains SEQ ID NOs 1, 2, etc. (so as to make clear the context for the limitations "56 base pairs upstream" and "62 base pairs downstream").

Claims 55 is indefinite over the references to "step (2)" in item (3) of the claim because the claim does not previously employ the term "step" or "step (2)" and does not otherwise make reference to method steps. This rejection could be overcome by, e.g., amending claim 55 to recite "comprising the steps of" (in lieu of "comprising" in line 3).

Claim 55 is indefinite over the recitation of the limitation "said nucleotide sequence of mycobacteria strains of M. tuberculosis complex" in item (1) of the claim because there is insufficient antecedent basis for this limitation. This rejection could be overcome by amending the claim to recite "said nucleotide sequence of mycobacteria of M. tuberculosis complex."

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claim 37 is rejected under 35 U.S.C. 102(b) as being anticipated by Blakely et al (US 5,418,162 A [5/1995]).

The claim is drawn to a nucleotide probe "that consists of 21 base pairs having a sequence of a region of sequence SEQ ID No: 2 comprising the GAG codon in positions 40 to 42 or the complement of said region." Thus, the claim broadly encompasses any 21mer probe "having a sequence" of "a region....comprising the GAG codon;" i.e., any 21mer. Blakely et al teach such a 21mer (SEQ ID NO: 12; also see Example 7 at col 15, line 55-col 16, line 27). Thus, Blakely et al anticipate the claim.

9. Claim 38 is rejected under 35 U.S.C. 102(b) as being anticipated by Brennan (US 5,474,796 A [12/1995]).

The claim is drawn to a nucleotide probe comprising a sequence "composed of nucleotides in positions 31 to 51 of SEQ ID No: 2 or the complement of said sequence." Brennan discloses an array of oligonucleotides comprising all possible 10-mers (see entire reference, particularly Example 4). Each of the probes of Brennan may be "composed of" the nucleotide present in positions 31 to 51 of SEQ ID No: 2. Accordingly, Brennan anticipates the claimed invention.

Allowable Subject Matter

10. Claims 36, 44, and 54 are allowed.

11. Claim 32 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday and Thursday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571/272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Diana B. Johannsen
Primary Examiner
Art Unit 1634